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## TITLE OF THE INVENTION

CO<sub>2</sub> INCUBATOR

#### BACKGROUND OF THE INVENTION

5 Field of the Invention

> The present invention relates to a CO2 incubator for incubating cells sampled from blood or a specimen by controlling a temperature, a humidity and an atmosphere of the cells.

10 Description of the Related Art

> In recent years, with the development of fields regarding biotechnology and regeneration medicine, works for incubating cells by using an incubator tend to increase. accelerate the incubation of the cells, it is necessary to regulate an incubation space suitable for each cell, and heretofore, some incubators have been developed which control a temperature, a humidity and an atmosphere in the incubation space.

Particularly, to incubate the cells which requires 20 severe concentration conditions of a CO2 (carbon dioxide) gas, a CO<sub>2</sub> incubator is used as a device for controlling the CO<sub>2</sub> gas concentration in the incubation space in addition to a device for controlling the temperature and the humidity (e.g., refer to Patent Document 1 and Patent Document 2).

25 [ Patent Document 1]

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Official gazette of Japanese Patent Application Laid-Open No. 9-23877

[ Patent Document 2]

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Official gazette of Japanese Patent Application Laid-Open No. 2000-93156

However, in the case of the conventional  $CO_2$  incubator, when a door is automatically or manually opened and closed,  $CO_2$  leaks to the outside from a storeroom of the  $CO_2$  incubator and the  $CO_2$  gas concentration in the storeroom fluctuates. Moreover, when the door is frequently opened and closed to put in or take out the incubation cells, the  $CO_2$  gas concentration in the storeroom fluctuates before the  $CO_2$  gas concentration in the storeroom returns to its predetermined concentration. Therefore, there is a problem that the state of the incubation space of the cells becomes unstable, which adversely affects the growth of the cells.

For the solution of the problem, in the case of the conventional  $CO_2$  incubator, a  $CO_2$  concentration sensor is disposed in the storeroom for the fluctuation of the  $CO_2$  gas concentration. In consequence, when the  $CO_2$  concentration is recognized to be lower than a set value in accordance with an output of the sensor, a switching valve for supplying the  $CO_2$  gas into the storeroom is opened, and when the  $CO_2$  concentration reaches the set value, the switching valve is closed.

In this case, the above conventional  $CO_2$  gas concentration sensor has a poor concentration detecting performance, and hence, a problem that the accuracy of the detected concentration is low, and moreover, a long time is

required to detect the concentration. In addition, an airtight structure is used to reduce a gas consumption, and if overshoot occurs, it takes a long time to return to a predetermined value. Therefore, there is no way other than an operation of decreasing a gas injection quantity to decelerate recovery. The above control is due to an imperfect performance of the sensor. In any case, when the switching valve for supplying the  $\mathrm{CO}_2$  gas is controlled in accordance with the output of the  $\mathrm{CO}_2$  gas concentration sensor as in the conventional case, a problem occurs that the actual  $\mathrm{CO}_2$  gas concentration overshoots or undershoots to the preset  $\mathrm{CO}_2$  gas concentration.

Therefore, there is a problem that it is difficult to realize the strict  ${\rm CO_2}$  gas concentration and it is impossible to sufficiently regulate the cell incubation space.

### SUMMARY OF THE INVENTION

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Therefore, the present invention has been developed to solve the above conventional technical problems, and an object of the present invention is to provide a  $CO_2$  incubator capable of accurately controlling a  $CO_2$  gas concentration in an incubation space and quickly coping with a sudden change of the  $CO_2$  gas concentration in the incubation space.

A first aspect of the present invention is directed to a  $CO_2$  incubator for incubating a culture medium accommodated in an incubation space defined in a storeroom, the  $CO_2$  incubator comprising  $CO_2$  gas concentration detection

means for detecting a  $CO_2$  concentration in the incubation space,  $CO_2$  gas concentration setting means for setting the  $CO_2$  gas concentration in the incubation space,  $CO_2$  gas supply means for supplying a  $CO_2$  gas into the incubation space, and control means for controlling the  $CO_2$  gas supply means, wherein the control means executes an operation of proportion, proportion and integration, or proportion and integration and differentiation on the basis of a deviation between the  $CO_2$  gas concentration in the incubation space and a set  $CO_2$  gas concentration value by the  $CO_2$  gas concentration detection means and the  $CO_2$  gas concentration setting means to calculate a  $CO_2$  gas supply time per unit time to the incubation space and a stop time, and supplies a  $CO_2$  gas to the incubation space from the  $CO_2$  gas supply means in accordance with the calculated supply time and stop time.

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According to the thus constituted first aspect of the present invention, overshoot and undershoot of the  $\rm CO_2$  gas concentration can be previously avoided by the above control means, whereby the  $\rm CO_2$  gas concentration can be accurately controlled.

In consequence, even if the  $CO_2$  gas concentration in the incubation space is extremely changed by opening or closing a door, the  $CO_2$  gas can be quickly supplied to the incubation space in accordance with the changed  $CO_2$  gas concentration in the incubation space, whereby the stable incubation space can be provided.

A second aspect of the present invention is directed

to the  ${\rm CO}_2$  incubator according to the first aspect of the present invention, wherein the  ${\rm CO}_2$  gas concentration detection means is constituted of a  ${\rm CO}_2$  sensor using infrared rays.

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According to the second aspect of the present invention, it is possible to further quickly and accurately detect the  $CO_2$  gas concentration in the incubation space, because the  $CO_2$  gas detection means is constituted of a  $CO_2$  sensor using infrared rays in the first aspect of the present invention.

A third aspect of the present invention is directed to the  $\mathrm{CO}_2$  incubator according to the first aspect or the second aspect of the present invention, wherein a plurality of incubation spaces are disposed and the control means selects the gas in any incubation space, detects the  $\mathrm{CO}_2$  gas concentration of the selected gas by the  $\mathrm{CO}_2$  gas concentration detection means, and controls the supply of the  $\mathrm{CO}_2$  gas to each incubation space in accordance with the detected  $\mathrm{CO}_2$  gas concentration.

According to the third aspect of the present invention, a plurality of incubation spaces are disposed and the control means selects the gas in any incubation space, detects the  $\rm CO_2$  gas concentration of the selected gas by the  $\rm CO_2$  gas concentration detection means, and controls the supply of the  $\rm CO_2$  gas to each incubation space in accordance with the detected  $\rm CO_2$  gas concentration in the first aspect or the second aspect of the present invention. Therefore,

the  $CO_2$  gas concentration can be controlled for each incubation space.

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Moreover, since the  $CO_2$  gas concentration detection means and the control means control the  $CO_2$  gas concentrations in the respective incubation spaces by using common means, it is possible to avoid a fluctuation of the  $CO_2$  gas concentration in each incubation space caused by an error of the  $CO_2$  gas concentration detection means or the control means, as compared with a case where the  $CO_2$  gas concentrations in the respective incubation spaces are controlled by the plurality of  $CO_2$  incubators.

A fourth aspect of the present invention is directed to the  $\mathrm{CO}_2$  incubator according to the third aspect of the present invention, wherein the control means displays the  $\mathrm{CO}_2$  gas concentration detected in each incubation space in the third aspect of the present invention.

According to the fourth aspect of the present invention, because the control means displays the  $CO_2$  gas concentration detected in each incubation space in the third aspect of the present invention, the  $CO_2$  gas concentration in each incubation space can be easily visually confirmed, whereby convenience is further improved.

### BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a schematic block diagram of a  ${\rm CO}_2$  incubator of the present invention showing the flow of air; and

FIG. 2 is a schematic block diagram of a  ${\rm CO}_2$  incubator of another embodiment showing the flow of air.

# DESCRIPTION OF THE PREFERRED EMBODIMENTS

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Next, an embodiment of the present invention will be described below in detail by referring to the accompanying drawings. FIG. 1 shows a schematic block diagram of a CO<sub>2</sub> incubator 1 of the present invention showing the flow of air. In the case of the CO<sub>2</sub> incubator 1 of the present invention, a body 2 is constituted of an adiabatic housing having an opening (not shown) on, for example, one face, and an incubation space S is defined in the body 2 (in the storeroom). Moreover, the body 2 is provided with a door, not shown, for closing the opening which can be opened and closed.

The body 2 is provided with an air-agitating blower 3 for agitating the air in the incubation space S to uniform the state of the air. It is to be noted that the air-agitating blower 3 is operated by a blower motor 3A, and the blower motor 3A is controlled by a controller not shown.

Moreover, the body 2 is connected to a measurement air sampling tube 4 so as to communicate with the inside of the incubation space S, and the measurement air sampling tube 4 is connected to a  $\rm CO_2$  gas concentration sensor 6 as  $\rm CO_2$  gas concentration detection means for detecting the  $\rm CO_2$  gas concentration in the incubation space S through a pump 5. The  $\rm CO_2$  gas concentration sensor 6 used in this embodiment

may be a  $CO_2$  sensor using infrared rays.

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This  $CO_2$  sensor using the infrared rays calculates the  $CO_2$  gas concentration by using a principle that the  $CO_2$  gas absorbs a wavelength of 4.3  $\mu m$ . That is to say, the  $CO_2$  sensor measures a wavelength absorbing degree, converts the measured data into an electrical signal, and calculates the  $CO_2$  gas concentration. Moreover, this  $CO_2$  sensor ( $CO_2$  gas concentration sensor 6) may be connected to a  $CO_2$  gas controller 11 which will be described later in detail.

Furthermore, the  $CO_2$  gas concentration sensor 6 is connected to a measurement air return tube 7 whose one end communicates with the inside of incubation space S of the body 2. In consequence, when the pump 5 is operated, the air taken by the  $CO_2$  gas concentration sensor 6 through the measurement air sampling tube 4 from the inside of the incubation space S is returned to the inside of the incubation space S through the measurement air return tube 7.

On the other hand, the body 2 is connected to a  $CO_2$  gas supply tube 8 so as to communicate with the inside of the incubation space S, and the  $CO_2$  gas supply tube 8 is connected to a  $CO_2$  gas cylinder 10 through an electromagnetic switching valve 9 as  $CO_2$  gas supply means. In this  $CO_2$  gas cylinder 10, the  $CO_2$  gas having a purity of 95% or more may be contained.

Here, the  $CO_2$  gas controller 11 will be described below. The input side of the  $CO_2$  gas controller 11 is connected to the  $CO_2$  gas concentration sensor 6 and a control

panel 12, and the output side of the  $CO_2$  gas controller 11 is connected to the electromagnetic switching valve 9.

The control panel 12 is provided with  $CO_2$  gas concentration setting means for setting the  $CO_2$  gas concentration in the incubation space S, and for example, the control panel 12 is disposed in front of the body 2. Moreover, the control panel 12 may be provided with a display portion 12A for displaying the actually detected  $CO_2$  gas concentration in the incubation space S and the set  $CO_2$  gas concentration.

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The CO<sub>2</sub> gas controller 11 controls the electromagnetic switching valve 9 as CO2 supply means in accordance with the CO2 gas concentration sensor 6 and control panel 12 and includes a PID-operation processing section 11A. The PID-operation processing section 11A executes operations of proportion (P), integration (I) and differentiation (D) on the basis of a deviation e between a CO2 gas concentration in the incubation space S detected by the  $CO_2$  gas concentration sensor 6 and a set  $CO_2$  gas concentration value which is optionally set by the control panel 12. That is, the PID-operation processing section 11A performs a proportional operation for calculating a control amount so as to reduce the deviation e in proportion to the deviation e between the CO2 gas concentration detected by the CO2 gas concentration sensor 6 and a set CO2 gas concentration value, an integral operation for calculating a control amount for reducing an integrated value of the

deviation e, and a differential operation for calculating a control amount for reducing a gradient (differentiated value) of a change of the deviation. Next, these control amounts are added together to calculate a  $CO_2$  gas supply time per unit time (every certain cycle of, e.g., 3 seconds) of the electromagnetic switching valve 9 and a stop time in accordance with the control amounts.

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Then, the CO<sub>2</sub> gas controller 11 controls the electromagnetic switching valve 9 as CO<sub>2</sub> gas supply means in accordance with the CO<sub>2</sub> gas supply time and the stop time calculated in accordance with the PID control and controls the supply of the CO<sub>2</sub> gas to the incubation space S from the CO<sub>2</sub> gas cylinder 10. In the case of this embodiment, operation processings of proportion, integration, and differentiation are performed in accordance with a deviation between a detected CO<sub>2</sub> gas concentration and a set CO<sub>2</sub> gas concentration set value to calculate a CO<sub>2</sub> gas supply time and a stop time. Moreover, it is allowed to calculate the CO<sub>2</sub> gas supply time and the stop time by executing operations of only proportion or operations of only proportion and integration in accordance with the deviation.

Operations of a CO<sub>2</sub> incubator will be described below in accordance with the above configuration. First, a user operates the control panel 12 to set the CO<sub>2</sub> gas concentration in the incubation space S. In this case, some air in the incubation space S is attracted into the measurement air sampling tube 4 by operating the pump 5 and

captured into the  $CO_2$  gas concentration sensor 6. Thereafter, the air used for measurement is returned to the incubation space S through the measurement air return tube 7.

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In this case, the CO<sub>2</sub> gas concentration sensor 6 measures the absorbance of a wavelength of 4.3  $\mu m$  by infrared rays to calculate a CO2 gas concentration. The CO2 gas controller 11 executes the above-described PID operation processing in accordance with the calculated CO2 gas concentration and the CO2 gas concentration set value set as described above. Moreover, the controller 11 calculates the  $CO_2$  gas supply time and the stop time per unit time in accordance with the PID operation processing and controls the electromagnetic switching valve 9 in accordance with the supply time and the stop time. Then, the controller 11 supplies the CO2 gas into the incubation space S through the  $CO_2$  gas supply tube 8 from the  $CO_2$  gas cylinder 10. gas supply quantity increases when the rate of the supply time in the above three secconds (supply time + stop time) rises but decreases when the rate lowers. operation is calculated every three sec to perform a fine control.

Thereby, it is possible to prevent overshoot and undershoot in the control of a  $CO_2$  gas concentration and accurately control the  $CO_2$  gas concentration in the incubation space S. Therefore, even if the  $CO_2$  gas concentration in the incubation space S is extremely changed by opening or closing the door, it is possible to quickly

supply the  $CO_2$  gas into the incubation space S in accordance with a changed  $CO_2$  gas concentration in the incubation space S and stably supply the incubation space S.

Particularly, because the  $CO_2$  gas concentration sensor 6 of this embodiment for detecting the  $CO_2$  gas concentration in the incubation space S is constituted of a  $CO_2$  sensor using infrared rays, it is possible to further quickly and accurately detect the  $CO_2$  gas concentration in the incubation space S.

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Then, another embodiment of the present invention is described below by referring to FIG. 2. FIG. 2 shows a schematic block diagram of a CO<sub>2</sub> incubator 20 of another embodiment of the present invention showing the flow of air. It is to be noted that the members having the same symbols as in FIG. 1 have similar effects.

In the case of the CO<sub>2</sub> incubator 20 of this embodiment, a body 22 is constituted of an adiabatic housing having an opening (not illustrated) on one face the same as the case of the above embodiment. Moreover, a partition wall 22 is formed in the inside (storeroom) of the body 22 and incubation spaces 1S and 2S divided by the partition wall 21 are also formed. Furthermore, the body 22 is provided with a not-illustrated door for blocking the incubation spaces 1S and 2S respectively so that the opening can be opened or closed.

On the other hand, the body 22 is connected with measurement air sampling tubes 4A and 4B so as to communicate

with insides of the incubation spaces S1 and S2, respectively, and these measurement air sampling tubes 4A and 4B are connected to a measurement air sampling tube 4 through a three-way tube 23. The measurement air sampling tube 4 connected to a CO<sub>2</sub> gas concentration sensor 6 as CO<sub>2</sub> gas concentration detection means for detecting the CO<sub>2</sub> gas concentration in the incubation space S1 of S2 through a pump 5. Also in the case of this embodiment, the CO<sub>2</sub> gas concentration sensor 6 may be a CO<sub>2</sub> sensor using infrared rays. Moreover, the CO<sub>2</sub> gas concentration sensor 6 may be connected to a CO<sub>2</sub> gas controller 25 which will be described later in detail.

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Furthermore, the CO<sub>2</sub> gas concentration sensor 6 is connected to a measurement air return tube 7, and the other end of the measurement air return tube 7 is connected to measurement air return tubes 7A and 7B communicating with the incubation spaces S1 and S2 through a three-way tube 24. In consequence, when the pump 5 is operated, the air selectively captured into the measurement air sampling tube 4 from the incubation space S1 or S2 is returned to the original incubation space S1 or S2 through the CO<sub>2</sub> gas concentration sensor 6 and measurement air return tube 7.

Furthermore, the body 22 is connected to CO<sub>2</sub> gas supply tubes 8A and 8B so as to communicate with the insides of the incubation spaces S1 and S2, and the CO<sub>2</sub> gas supply tubes 8A and 8B are connected to a CO<sub>2</sub> gas cylinder 10 through electromagnetic switching valves 9A and 9B as CO<sub>2</sub> gas

supply means.

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The  $CO_2$  gas controller 25 will be described below. The input side of the  $CO_2$  gas controller 25 is connected to the  $CO_2$  gas concentration sensor 6 and control panel 12, and the output side of the  $CO_2$  gas controller 11 is connected to the three-way valves 23 and 24 and the electromagnetic switching valves 9A and 9B.

The control panel 12 serves as  $CO_2$  gas concentration setting means for setting the  $CO_2$  gas concentration in each of the incubation spaces S1 and S2 the same as the case of the above embodiment and is set to, for example, the front of the body 2. Furthermore, the control panel 12 may be provided with display portions 12A and 12B for displaying an actually detected  $CO_2$  gas concentration in each of the incubation spaces S1 and S2 and a set  $CO_2$  gas concentration.

The  $\mathrm{CO}_2$  gas controller 25 includes a PID-operation processing section 25A therein as in the  $\mathrm{CO}_2$  gas controller 11 of the above embodiment, and controls the electromagnetic switching valve 9A or 9B as the  $\mathrm{CO}_2$  supply means by the  $\mathrm{CO}_2$  gas concentration sensor 6 for detecting the  $\mathrm{CO}_2$  gas concentration of the air in selected one of the incubation spaces S1 and S2 and the control panel 12 as the  $\mathrm{CO}_2$  gas concentration setting means. It is to be noted that the PID-operation processing section 25A may have the same constitution as the PID-operation processing section 11A of the above embodiment.

Operations of the CO2 incubator 20 of the present

invention will be described below in accordance with the above configuration. First, a user operates the control panel 12 to set the  $CO_2$  gas concentration in the incubation space S1 and/or S2. The  $CO_2$  gas concentration controller 25 selects either of the incubation spaces S1 and S2 and opens one of the three-way valves 23 and 24 and closes the other so as to make it possible to sample the air in the selected incubation space S1 or S2.

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Thereafter, some of the air in the selected incubation space S1 or S2 is attracted into the measurement air sampling tube 4 by operating the pump 5 and captured into the  $\rm CO_2$  gas concentration sensor 6. Then, the air used for measurement is returned to the original incubation space S1 or S2 through the measurement air return tube 7.

In this case, the  $CO_2$  gas concentration sensor 6 measures the absorbance of a wavelength of 4.3  $\mu m$  with infrared rays and calculates a  $CO_2$  gas concentration. Then, the  $CO_2$  gas controller 25 performs the PID control the same as the case of the above embodiment in accordance with the calculated  $CO_2$  gas concentration and a preset  $CO_2$  gas concentration set value, calculates the  $CO_2$  gas supply time and the stop time for each based unit time, and controls the electromagnetic switching valve 9A or 9B corresponding to the selected incubation space S1 or S2 in accordance with the calculated supply time and stop time. Moreover, the controller 25 supplies the  $CO_2$  gas to the incubation space S1 or S2 from the  $CO_2$  gas cylinder 10 through the  $CO_2$  gas supply

tube 8A or 8B.

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According to the above configuration, it is possible to avoid overshoot or undershoot through the control of the  $CO_2$  gas concentration in each of the incubation spaces S1 and S2 and accurately control the  $CO_2$  gas concentration in each of the incubation spaces S1 and S2. Therefore, even if the  $CO_2$  gas concentration in the incubation spaces S1 and S2 is extremely changed by opening or closing the door, it is possible to quickly supply the  $CO_2$  gas to the incubation spaces S1 and S2 in accordance with the changed  $CO_2$  gas concentration in each of the incubation spaces S1 and S2 and provide stable incubation spaces S1 and S2.

Moreover, even in the case of the  $CO_2$  incubator 20 in which a plurality of incubation spaces are defined as in this embodiment, the  $CO_2$  gas concentration in each of the incubation spaces S1 and S2 can be controlled by using the common pump 5, the  $CO_2$  gas concentration sensor 6 and the  $CO_2$  gas controller 25, whereby a plurality of types of incubation spaces can be defined in one  $CO_2$  incubator 20.

Particularly in the above case, because a  $CO_2$  gas concentration can be controlled by using the common  $CO_2$  gas concentration sensor 6 and  $CO_2$  gas controller 25, it is possible to avoid the fluctuation of the  $CO_2$  gas concentration in a incubation space caused by an error of  $CO_2$  gas concentration detection means or control means compared to the case of controlling the  $CO_2$  gas concentration in each of the incubation spaces S1 and S2 by a plurality of  $CO_2$ 

incubators.

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Moreover, because the control panel 12 of this embodiment is provided with the display portions 12A and 12B for displaying the  $CO_2$  gas concentrations detected in the respective incubation spaces S1 and S2, the  $CO_2$  gas concentrations in the respective incubation spaces S1 and S2 can be easily visually confirmed, whereby convenience is further improved.

With regard to the  $\mathrm{CO}_2$  incubators 1 and 20 of the above embodiments, reference has been made to the  $\mathrm{CO}_2$  gas concentration control alone in the incubation spaces S1 and S2. However, it is also allowed to use an incubator making it possible to control an environment required to incubate cells such as temperature control and humidity control in each of the incubation spaces S1 and S2.

As described above, according to the present invention, a  $CO_2$  incubator for incubating a culture medium accommodated in an incubation space defined in a storeroom comprises  $CO_2$  gas concentration detection means for detecting a  $CO_2$  concentration in the incubation space,  $CO_2$  gas concentration setting means for setting the  $CO_2$  concentration in the incubation space,  $CO_2$  gas supply means for supplying the  $CO_2$  gas into the incubation space, and control means for controlling the  $CO_2$  gas supply means, wherein the control means executes an operation of proportion, proportion and integration, or proportion and integration on the basis of a deviation between the  $CO_2$ 

gas concentration in the incubation space and a set  $CO_2$  gas concentration value by the  $CO_2$  gas concentration detection means and the  $CO_2$  gas concentration setting means to calculate a  $CO_2$  gas supply time per unit time to the incubation space and a stop time, and supplies the  $CO_2$  gas to the incubation space from the  $CO_2$  gas supply means in accordance with the calculated supply time and stop time. Accordingly, overshoot and undershoot of the  $CO_2$  gas concentration can be previously avoided, whereby the  $CO_2$  gas concentration can be accurately controlled.

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Consequently, even if the  $CO_2$  gas concentration in the incubation space is extremely changed, e.g., by opening or closing a door, the  $CO_2$  gas can be quickly supplied to the incubation space in accordance with the changed  $CO_2$  gas concentration in the incubation space, whereby the stable incubation space can be provided.

According to the invention of claim 2, the  $CO_2$  gas concentration detection means is constituted of a  $CO_2$  sensor using infrared rays in the invention of claim 1, and hence, the  $CO_2$  gas concentration in the incubation space can be further quickly and accurately detected.

According to the invention of claim 3, a plurality of incubation spaces are disposed, and the control means selects any gas in any incubation space, detects the  $CO_2$  gas concentration of the selected gas by the  $CO_2$  gas concentration detection means, and controls the supply of the  $CO_2$  gas to each incubation space in accordance with the

detected  $CO_2$  gas concentration. Accordingly, it is possible to control the  $CO_2$  gas concentration in each incubation space.

Moreover, because the  $CO_2$  gas concentration detection means and the control means control the  $CO_2$  gas concentration in each incubation space by using common means, it is possible to previously avoid the fluctuation of the  $CO_2$  gas concentration in an incubation space caused by an error of the  $CO_2$  gas concentration detection means or the control means, as compared with the case of controlling  $CO_2$  gas concentrations in the incubation spaces by a plurality of  $CO_2$  incubators.

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According to the invention of claim 4, the control means displays the  $CO_2$  gas concentration detected in each incubation space in the invention of claim 3, and hence, the  $CO_2$  gas concentration in each incubation space can be easily visually confirmed, whereby convenience is further improved.